

## Effekt av diett på mikrobiota

The diagram illustrates the effect of diet on microbiota, divided into four quadrants around a central circle with a clockwise arrow. Each quadrant is associated with a list of dietary factors.

- Dysbiosis Pathobionts** (Top Left, Orange):
  - High Fat/High Sugar Diet
  - High Fat diet
  - Gluten
  - Emulsifiers
  - Fosforyl
  - Low Fiber
- Metabolome** (Top Right, Red):
  - Low Fiber
  - Low Resistant Starch
  - High Fat
  - High Animal Protein
- Virulence Pathogenicity** (Bottom Left, Green):
  - Emulsifiers
  - Maltodextrins
  - High Fat (bile acids)
- Mucosal Adhesion Translocation** (Bottom Right, Purple):
  - Maltodextrins
  - Emulsifiers
  - Low Fiber
  - High Fat/High sugar

Logo: Akershus Universitetssykehus

# Diett og konsekvenser på immunsystemet

**Top-Left Quadrant (Dark Blue):** Mucous Layer Goblet Cells

- High Fat High Sugar Diet
- Emulsifiers
- Low Fiber

**Top-Right Quadrant (Grey):** Tregs Cathelicidins Defensins

- Low Fiber
- High Fat
- Gluten

**Bottom-Left Quadrant (Light Blue):** Intestinal Permeability

- Emulsifiers
- Carrageenans
- Gluten
- High Fat diet
- Alcohol

**Bottom-Right Quadrant (Medium Blue):** Intracellular Bacterial Clearance

- High Fat diet
- Maltodextrins

**Source:** Levine A et al. *Gut* 2018. *Evolving role of diet in the pathogenesis and treatment IBD.*

The diagram illustrates the differences in the gut microbiome and host response between Healthy individuals and those with Inflammatory bowel disease (IBD).

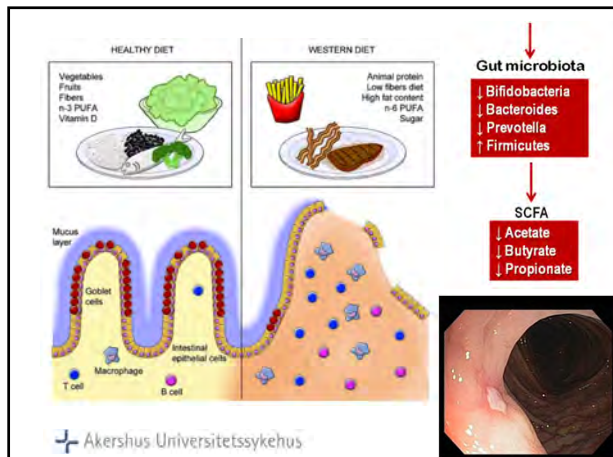
**Healthy:**

- SCFAs production: High
- Bile acid metabolism: High
- Vitamin production: High
- Microbiome: Diverse (high  $\alpha$ -diversity), including beneficial bacteria.
- Host Response: Integrity of mucosal barrier  $\uparrow$ , Treg  $\uparrow$ , Anti-inflammatory cytokines  $\uparrow$ .
- Outcome: Intestinal homeostasis.

**Inflammatory bowel disease (IBD):**

- SCFAs production: Low
- Bile acid metabolism: Low
- Vitamin production: Low
- Microbiome: Less diverse (low  $\alpha$ -diversity), with increased pathobionts and decreased beneficial bacteria.
- Host Response: Integrity of mucosal barrier  $\downarrow$ , Th1  $\uparrow$ , Th17, Pro-inflammatory cytokines  $\uparrow$ .
- Outcome: Intestinal inflammation.

**Source:** K. Sugihara, Diet-Microbiota Interactions in IBD, *Nutrients* 2021



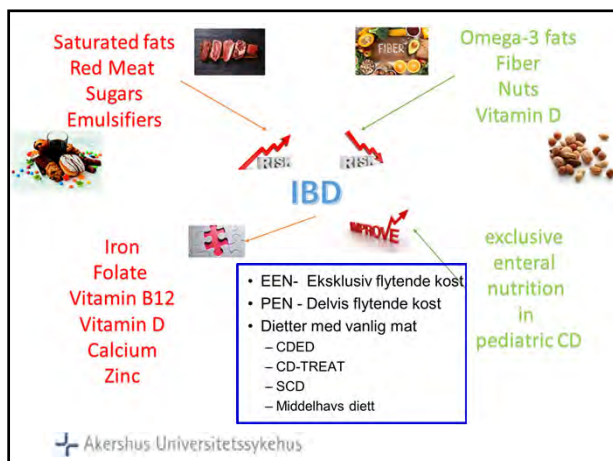
## Exclusive enteral nutrition= EEN

- Gullstandard Crohn hos barn
- Kur
- Fullverdig flytende kost som eneste næring
- "Flytende plaster"
- Fører til slimhinne tilheling
- Ingen bivirkninger bortsett fra compliance
- Remisjon hos 75-85% av pediatriske CD



Van Rheenen et al. The Medical Management of Paediatric Crohn's Disease: An ECCO-ESPGHAN Guideline Update. JCC 2020.  
Borrelli et al. Gastro Hepatol 2008

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## EEN vs steroider hos barn

- EEN mer effektiv til å indusere remisjon
- EEN er steroid besparende



Grover, Z et al. Two-Year Outcomes After EEN Induction Are Superior to Corticosteroids in Pediatric Crohn's Disease Treated Early with Thiopurines. Dig.Dis.Sci. 2015  
Connors. EEN Therapy in Paediatric Crohn's Disease Results in Long-term Avoidance of Corticosteroids. JCC 2017.  
Cohen-Dolev, N et al. Differences in Outcomes Over Time With EEN Compared With Steroids in Children With Mild to Moderate Crohn's Disease. JCC 2018

Diet	Intervention	Personalized
EEN	Liquid formula-based diet delivered to the gastro-intestinal tract orally or through nasogastric feeding.	No
PEN	Whole food diet supplemented with liquid formula-based diet for a prespecified percentage of calories.	No
SCD	Restriction of complex carbohydrates and elimination of refined sugar.	No
CD-ED	Exclusion of gluten and gluten-free baked goods, dairy products, animal fat, processed meats, emulsifiers, canned goods, and all packaged products with a due date. Restrictions can be loosened after 6 weeks.	No
CD-TREAT	Exclusion of gluten, lactose, and alcohol and matching of macronutrients, vitamins, minerals, and fibre with ordinary foods and multivitamin tablets, guided by personal preference.	Yes

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## Gutt 12 år

- Hanglet 6 mnd
  - klarer ikke gå til skolen, sluttet med fotball
- Failure to thrive
- Økende tømninger, blod, slim, nattlige
- Anemisk, høye inflammasjonsmarkører
  - Hb 9, SR 38, Crp 80
  - Fekal kalprotektin 1600



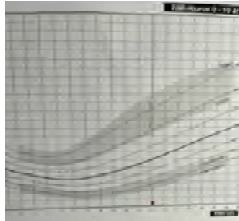
= Mb Crohn



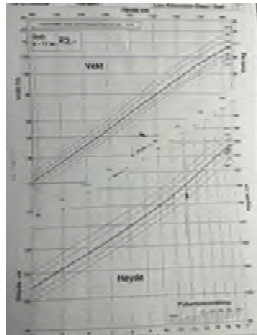
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12 ÅR, 24 kg, lengde 145 cm:  
6 kg under 3 persentilen

Underviktig  
Avflatende høyde  
Tapt > 10% av kroppsvekt



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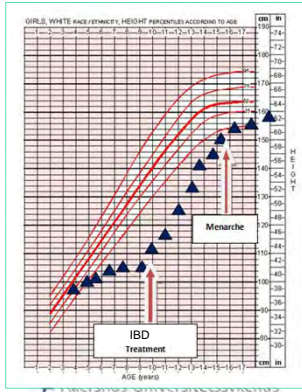
## Pediatrik CD

- Haster å få til remisjon  
– Unngå steroider
- Følger vekst, pubertet, utvikling

EEN 2 uker, v/ respons CDED 6 uker



## Hva er spesielt med barne-IBD?



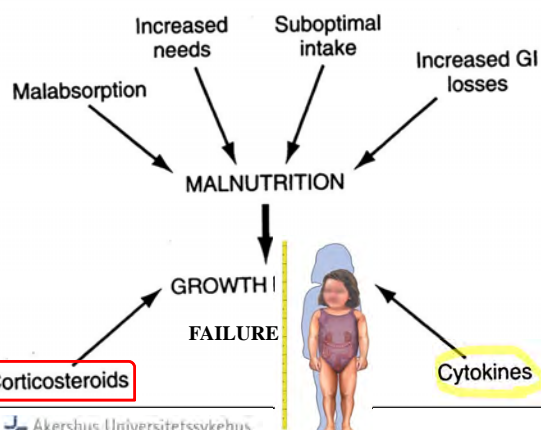
- Aggressiv
- Pubertet, vekst, utvikling



- Fullverdige næringsdrikker/sondenæring
- Obs refeeding
- Pasienten skal ikke være sulten



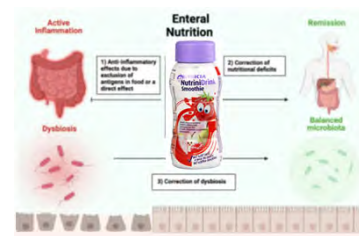
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## EEN

Respons ila 2-3 uker



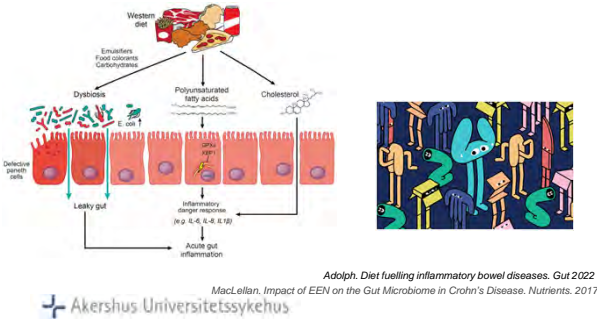
Sigall-Boneh et al. Dietary Therapies Induce Rapid Response and Remission in Pediatric Patients With Active Crohn's Disease. Clin Gastro Hep 2021

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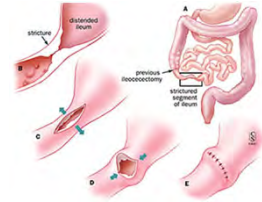
### Virkningsmekanismer ved EEN?

- Forbedrer ernæringsstatus, mangeltilstander, anti-inflammatorisk
- **Utelater diettkomponenter** som gir dysbiose/forstyrret immunsystemet/ LEAKY GUT



### Ernæring som behandling

- Induksjon ved CD
- Som tilleggsbehandling
- Preoperativt/ Postoperativt
  - Minsker septske komplikasjoner
  - Kan behandle komplikasjoner
- "Kirurgi sparende" effekt
- Kan gjentas som kur
  - dersom man er diett responder



Heenasing. EEN provides an effective bridge to safer interval elective surgery for adults with Crohn's disease. APT 2017  
Sigal-Dorosh. Dietary Therapy with the CDIED is a Successful Strategy for Induction of Remission in Children and Adults Failing Biological Therapy. JCC 2017.  
Wall G et al WJG 2013. Use of EEN in adults with Crohn's disease: a review.  
Li G. Preoperative EEN reduces the postoperative septic complications of fistulizing Crohn's disease. 2014. Eur J Clin Nutr.  
Wong JJ. Impact of Preoperative EEN on Postoperative Complications and Recurrence After Bowel Resection in Patients with Active Crohn's Disease. World J Surg.

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### EEN hos voksne

- Virker hos voksne
  - Reduserer inflammasjon og induserer mukosal healing
  - Studier viste signifikant bedring etter 2 uker
- Færre studier
- Tidligere studier vist bedre effekt av steroider vs EEN hos voksne
  - pga compliance?
  - Ikke støtte fra tverrfaglige team?
- Renaissance etter at vi har «funnet et nytt organ»- gutt mikrobiota

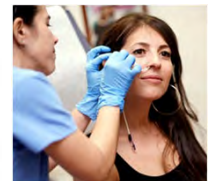


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Wall CL. Treatment of active CD with exclusive and partial enteral nutrition: a pilot study in adults. Inflamm Intest Dis 2018.

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### EEN spesielle indikasjoner

- Liquid Diet**
- if you have severe inflammation
  - before/after surgery
  - 2-8 weeks at a time"



S. Shariff. Current Use of EEN in Pre-Operative Optimisation in Crohn's Disease. Nutrients 2021  
Yang Q. Twelve-week peptide-based formula therapy may be effective in inducing remission of active Crohn disease among women who are pregnant or preparing for pregnancy. Nutr Clin Pract. 2021.

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### Polymerisk vs elemental

- Cochrane review: metaanalyse 27 studier
- Voksne CD pasienter
- Ingen forskjell i remisjonsrate
  - 64% remisjon elemental
  - 62% polymerisk
- Ingen forskjell i bivirkninger



Narula N et al. Enteral nutritional therapy for induction of remission in Crohn's disease. Cochrane 2018

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### EEN virker. Hva med PEN?

#### Partiell enteral nutrisjon

- Lik respons rate ved EEN og PEN
- Dersom diett er restriktiv



L. González-Torres et al. The Role of Partial Enteral Nutrition for Induction of Remission in Crohn's Disease. Nutrients 2022  
Limketkai et al. Dietary interventions for treatment of IBD. Clin Gastro Hep 2022

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## PEN som vedlikehold

- 35% av kalorier bør komme fra EN
  - Gkikas 2020
- Espghan anbefaler minst 50% EN for vedlikehold av remisjon



K. Gkikas. Dietary Strategies for Maintenance of Clinical Remission in IBD: Nutrients 2020

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## CEDED har 5 obligatoriske matvarer + 50% EEN



Tillatt: hvit ris, rismel, risnudler, urtete, ferskpresset appelsinjuice

Levine A et al. CEDED plus partial enteral nutrition induces sustained remission in a RCT. Gastroenterology 2019.

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PEN	Whole food diet supplemented with liquid formula-based diet for a prespecified percentage of calories.	No
SCD	Restriction of complex carbohydrates and elimination of refined sugar.	No
IgG-guided exclusion	Exclusion of foods with high serum anti-IgG titers.	Yes
CEDED	Exclusion of gluten and gluten-free baked goods, dairy products, animal fat, processed meats, emulsifiers, canned goods, and all packaged products with a due date. Restrictions can be loosened after 6 weeks.	No
CD-TREAT	Exclusion of gluten, lactose, and alcohol and matching of macronutrients, vitamins, minerals, and fibre with ordinary foods and multivitamin tablets, guided by personal preference.	Yes

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## CEDED hos voksne



- 47 barn og voksne med mild-moderat CD
  - Klinisk remisjon hos 70%, fall i CRP, SR, og mukosal tilheling
- 21 CD pas feilet biologisk behandling/kombo terapi
  - Klinisk remisjon hos 61%, fall i biomarkører
- Effekt av CEDED hos voksne med mild/moderat CD
  - 68% remisjon, mukosal tilheling

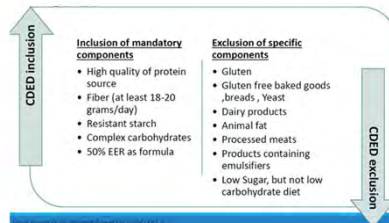
Sigal-Boneh. Partial enteral nutrition with a CEDED is effective for induction of remission in children and young adults with Crohn's disease. IBD 2014.

Sigal-Boneh. Dietary Therapy with the CEDED is a Successful Strategy for Induction of Remission in Children and Adults Failing Biological Therapy. JCC 2017.

Yanai H. CEDED for induction and maintenance of remission in adults with mild-to-moderate Crohn's disease Lancet Gastro Hep 2022.

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## PEN + CEDED; Crohn's disease exclusion diet



MODULife

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## «Vanlig mat» som diett??

- CEDED fase 2 og 3
- CD- TREAT
- SCD
- Middelhavsdiett
- Glutenfri
- FODMAP



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### The Crohn's disease treatment-with-eating diet (CD-TREAT)

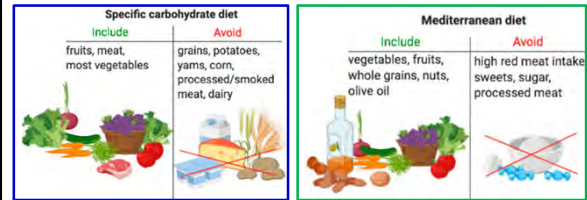
- **Whole food**
- Etterligner EEN (Modulen IBD) med vanlig mat
- **CD- TREAT forandrer microbiota slik som EEN**
- Uten gluten, laktose, alkohol
- Maltodextrin byttet ut med stivelsesrike matvarer
- Mer protein
- Multivitamin tablet
- Både CD-TREAT og EEN minsker SCFA men synes å virke likevel???



Svalos, V et al. Treatment of Active Crohn's Disease With an Ordinary Food-based Diet That Replicates EEN. Gastroenterology 2019  
Logan, M et al. Analysis of 61 EEN formulas used in the management of active Crohn's disease-new insights into dietary disease triggers. APT. 2020

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### SCD ikke bedre enn middelhavsdiett



Dine -CD: 194 CD pas enten SCD eller MD:  
Lewis et al. Comparing the specific carbohydrate diet to a Mediterranean diet in adults with Crohn's disease. Gastroenterology 2021

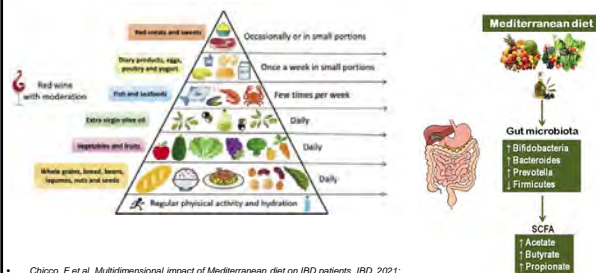
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### Middelhavs diett

har mye fiber- prebiotika, øker SCFA- føde for enterocytter



Chico, F et al. Multidimensional impact of Mediterranean diet on IBD patients. IBD. 2021:  
- Bedret nutrisjon, BMI, leversteatose, mindre aktiv sykdom  
- bedre inflammasjonsmarkører hos UC og CD pas

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### SCD: Veldig restriktiv

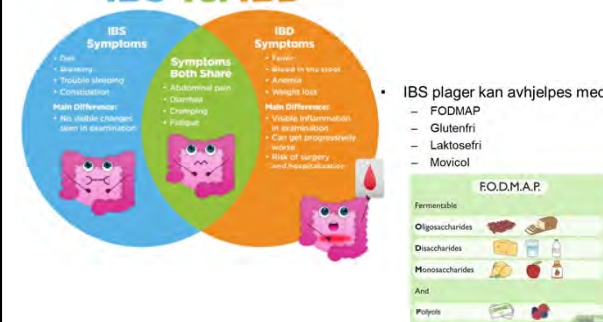
- Kun monosakkarider
- Ikke di- eller polysakkarider
- Ikke kornprodukter
- Ikke mais, ris, quinoa
- Ikke melkeprodukter
  - Kun fermenterte og harde oster
- Vist effekt (få pasienter)
- Obs mangeltillstander



Suskind. The Specific Carbohydrate Diet and diet modification as induction therapy for pediatric Crohn's disease. Nutrients 2020.


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### IBS vs. IBD



Pedersen et al. Low-FODMAP diet reduces IBS in patients with IBD. WJG 2017

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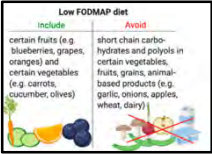


**Gluten-free diet**

**Include:** all non-gluten containing foods, including potatoes, maize, soy, rice, etc.

**Avoid:** gluten-containing grains: wheat, rye, barley, oats, etc.

- **Gluten fri-**
  - ingen effekt på IBD inflammasjon



**Low FODMAP diet**

**Include:** certain fruits (e.g. blueberries, grapes, oranges) and certain vegetables (e.g. carrots, cucumber, olives)

**Avoid:** short chain carbohydrates and polyols in certain vegetables, fruits, grains, animal-based products (e.g. garlic, onion, apples, wheat, dairy)

- **FODMAP**
  - Ingen effekt på IBD inflammasjon
  - Obs forandrer mikrobiota
    - pga lite komplekse KH
  - Ikke langvarig, best v inaktiv sykdom

Linket al BN. Dietary interventions for induction and maintenance of remission in IBD. Cochrane 2019.

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## Diett og IBD

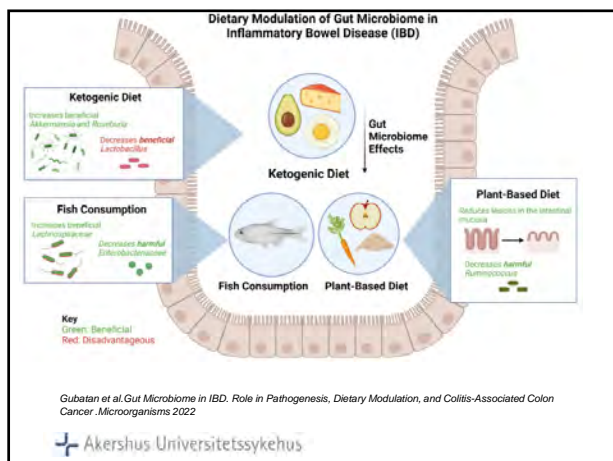
**Hva vet vi**

- Vestlig diett gir økt IBD
- Diett + Mikrobiota = sant
- EEN
  - Effekt barn+voksne med CD
- PEN
  - som vedlikehold
- Diett
  - Kan virke hvis restriktiv

**Hva vet vi ikke**

- Hvorfor virker EEN?
  - Når EEN har emulgatorer
  - Når det reduserer SCFA
- Effekt av »Whole food«
- Individualisert diett
- UC og diett

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## https://niscg.no online plattform IBD

**NISG**  
Norwegian IBD Study Group

**Om NISG**  
Om NISG  
Hvordan kontakte NISG

**Om IBD**  
Hva er IBD?  
Hva er Crohns sykdom?  
Hva er ulcerøs kolitt?

**Utdanning**  
IBD Updates  
Kongresser, møter og kurs  
Kommende prosjekter

**Forskning**  
Forskningssjupper i Norge  
Sjupper

**Arbeidsgrupper**  
(under utvikling)

**IBD Bildeatlas**  
IBD Bildeatlas  
IBD i endoskopi  
Histologi  
Histologi

**Pasientområde**  
IBD Skolen

→ Kongresser, møter & kurs  
≡ LUKK MENY

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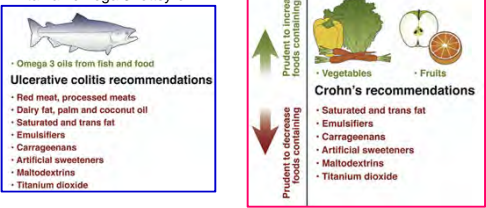
## Diett anbefalinger IBD

IBD

- Spis komplekse KH
- Eliminer transfett og mettede fettsyrer
- Unngå tilsetningsstoffer
  - Maltodextrin, emulgatorer, carrageenan, kunstig søtningsmiddel, tykningsmiddel

UC:

- Mindre rødt kjøtt
- Reduser palmeolje, kokosolje, melkeprodukter
- Øk inntak av omega 3 fettsyrer



**Ulcerative colitis recommendations**

- Omega 3 oils from fish and food
- Red meat, processed meats
- Dairy fat, palm and coconut oil
- Saturated and trans fat
- Emulsifiers
- Carrageenans
- Artificial sweeteners
- Maltodextrins
- Titanium dioxide

**Crohn's recommendations**

- Vegetables
- Fruits
- Saturated and trans fat
- Emulsifiers
- Carrageenans
- Artificial sweeteners
- Maltodextrins
- Titanium dioxide

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Levine A. Dietary guidance from IOIBD. Clin Gastro Hep 2020

## Oppsummert

- Økende IBD forekomst parallelt med vestlig diett
- Tarmbakterier og kost er viktig!




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## Referanser

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- Narula N, Dillon A, Zhang D, Shewlock ME, Tondeur M, Zachos M. Enteral nutritional therapy for induction of remission in Crohn's disease. The Cochrane database of systematic reviews. 2018;4.Cd000542.
- Sigall-Boneh R, Pfeffer-Glik T, Segal I, Zangen T, Boaz M, Levine A. Partial enteral nutrition with a Crohn's disease exclusion diet is effective for induction of remission in children and young adults with Crohn's disease. Inflamm Bowel Dis 2014;20:1353-60.
- Levine A, Wine E, Assa A, Sigall Boneh R, Shaoul R, Kori M, et al. Crohn's Disease Exclusion Diet Plus Partial Enteral Nutrition Induces Sustained Remission in a Randomized Controlled Trial. Gastroenterology. 2019;157(2):440-50.e8.
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- Limketkai BN, Iheozor-Ejiofor Z, Giuladin-Hellon T, et al. Dietary interventions for induction and maintenance of remission in inflammatory bowel disease. Cochrane Database Syst Rev 2019; 2019:CD012839.
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